Leda Dunn Wettre, Esq.
Michael J. Gesualdo, Esq.
ROBINSON, WETTRE & MILLER LLC
One Newark Center, 19th Floor
Newark, New Jersey 07102
Telephone: (973) 690-5400
Facsimile: (973) 466-2760
lwettre@rwmlegal.com

OF COUNSEL:
William G. Gaede III, Esq. (*pro hac vice*)
David L. Larson, Esq. *(pro hac vice)*
Bhanu K. Sadasivan, Esq. (*pro hac vice*)
Shane G. Smith, Esq. *(pro hac vice)*
Daniel K. Greene, Esq. (*pro hac vice*)
McDERMOTT WILL & EMERY LLP
275 Middlefield Road, Suite 100
Menlo Park, CA 94025-4004
Telephone: (650) 815 7400
Facsimile: (650) 815-4701

Attorneys for Plaintiff Depomed, Inc.

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

DEPOMED, INC., Plaintiff, v. ACTAVIS ELIZABETH LLC, *et al.*, Defendant.	No: 3:12-CV-01358 JAP (TJB) **PLAINTIFF DEPOMED, INC.'S TRIAL BRIEF** **Honorable Joel A. Pisano** Trial Date: May 12, 2014

PUBLIC VERSION

TABLE OF CONTENTS

Page

TABLE OF AUTHORITIES

Page

CASES

TABLE OF AUTHORITIES
(continued)

Page

TABLE OF AUTHORITIES
(continued)

Page

STATUTES

RULES

I. INTRODUCTION

In this Hatch-Waxman case, plaintiff Depomed asserts infringement of seven patents listed in the Orange Book for its branded pharmaceutical dosage form called Gralise®, which was approved in January 2011 for the treatment of post-herpetic neuralgia (PHN). Gralise® is a novel solid oral dosage form for once-daily administration of gabapentin that is gastrically (stomach) retained while the gabapentin is released. That active ingredient was previously available only in a thrice-daily, immediate release dosage form as Neurontin, which was originally approved in 1993 for treatment of epilepsy (and later approved after filing of the patents-in-suit for PHN). Defendants Actavis Elizabeth LLC and Actavis LLC ("Actavis"), based on ANDA No. 203611, seek to market a generic, once-daily bioequivalent product to Gralise® in both 300mg and 600mg tablets.

Actavis does not dispute infringement of two of the seven asserted patents. Actavis disputes that it infringes the "gastric retention" claim element common to four of the remaining patents, and disputes that its dosage forms are "an oval" as required by the seventh patent.

Actavis alleges an obviousness defense to six of the patents. For the seventh patent, Actavis has filed a motion seeking to amend its invalidity contentions to add an indefiniteness challenge on a claim element which has been construed by this Court. Depomed urges the Court to deny that motion.

A full list of the legal issues to be decided is set forth in Depomed's and Joint Legal Issues filed with Joint Pretrial Order. Briefly, the primary issues the Court must decide include:

Infringement of '280, '927, '989, and '756 Patents

1. Whether the 300mg and 600mg dosage forms proposed in Actavis' ANDA are "such that when the dosage form is introduced into the stomach in the fed mode, the dosage form remains in the stomach for several hours." ECF 251 (Claim Construction Order) at 7-8.

[redacted]

Actavis further disputes that the requirements of inducing and contributory infringement are met for the '927 and '756 Patents' method claims. The dosage

forms when administered with the Actavis label establish inducing infringement and the Actavis dosage forms have no substantial noninfringing uses where the method claims are directed to a "therapeutic effect" or "neuropathic pain."

Actavis further seeks to reconstrue the functional claim element in the '280 Patent "[the dosage form] is of a size exceeding the pyloric diameter in the fed mode to promote retention in the stomach during said fed mode." As stated above, the Court construed this element to mean "such that when the dosage form is introduced into the stomach in the fed mode, the dosage form remains in the stomach for several hours." ECF No. 251. Defendants now wish to read in an additional requirement in this patent only that the dimensions of the dosage form "must be of a size that is larger than the pyloric diameter in the fed mode." As reflected in this Court's *Markman* Order, this additional limitation resurrects Defendants' rejected construction that the dosage form "*is of a size exceeding the pyloric diameter in the fed mode* such that when introduced into the stomach in the fed mode, the dosage form remains in the stomach for the duration of drug delivery." ECF No. 251 at 7-8.

Consistently, this Court and other courts have construed this element functionally as the Court did in its *Markman* Order, and Actavis did not move for reconsideration. Notably, Judge Breyer of the Northern District of California

explained that a special meaning need not be ascribed to this claim term, which is found in the '280 Patent claims, but not in the now unasserted '475 Patent claims:

> The Court is unpersuaded that the specific language in the '280 patent regarding the expansion of the dosage form to a 'size exceeding the pyloric diameter' should render the meaning of that term different in substance from the term in 475 patent, which refers only more generally to a 'size large enough to promote retention in the stomach.' Indeed, the equivalence of these two phrases is evident from the plain language of the '280 patent itself, which suggests that a swollen dosage form must achieve a size exceeding the pyloric diameter precisely in order to promote its retention in the stomach.

ECF No. 138-2, Ex. 10 (Judge Breyer's Construction) at 16.

Actavis lacks basis to add a new requirement on the Court's construction that already considered the element and construed it functionally.

Infringement of the '962 Patent

> 2. Whether the 600mg Actavis dosage form is one "wherein said matrix has a shape which when projected onto a plane, is either an oval or a parallelogram".

The evidence will show that the matrix of the 600 mg Actavis tablet projects "an oval" as defined by the parties' stipulated construction: "any curve that is closed and concave towards the center wherein the geometric form bounded by the closed curve has a first and second orthogonal axes of unequal length." This was the construction Judge Hamilton rendered in *Depomed v. Lupin*, Case No. C-09-5587, 2011 U.S. Dist. LEXIS 52839 (N.D. Cal. May 17, 2011) and this Court ordered in *Depomed v. Sun*, Case 3:11-CV-03553 JAP (TJB). Actavis expert David Friend did not apply the parties' agreed construction in his rebuttal report, a

fact he expressly admitted in deposition. Nor did Actavis assert that it contested noninfringement of this element in its noninfringement contentions. ECF No. 278 (Greene Declaration in Support of Depomed's Motion in Limine Nos. 1-6), Ex. 1 at 10. The Court should bar Actavis from arguing for a different construction of "oval" or proferring new evidence on the subject at trial and should further be precluded for violating the local patent rules on failing to disclose this element as contested.

Validity of the '280 Patent

> 3. Whether the Court should permit Actavis to amend its invalidity contentions to argue indefiniteness against the '280 Patent, and if so, whether the claim term "a size that exceeds the pyloric diameter in the fed mode to promote retention in the stomach during said fed mode" is insolubly ambiguous.

The Court should deny Actavis' untimely motion to add a new ground of invalidity because Actavis cannot reasonably claim to have discovered the alleged indefiniteness after 20 months of litigation, and because Actavis never raised this issue during claim construction. In any event, this claim term has been judicially construed several times, and no Actavis expert claimed that they could not understand the term in an expert report or at deposition. On this record Actavis cannot clearly and convincingly establish the term as indefinite, nor that the '280 Patent is invalid.

Validity of the '962 Patent

4. Whether the asserted claims of the '962 Patent are rendered obvious by a combination of the WO '107, WO '128, WO '360, the '843 Patent (aka Curatolo) and/or WO '285 references.

Actavis cannot clearly and convincingly demonstrate that the '962 Patent is obvious because no reference cited by Actavis, either alone or as combined by Actavis (i) addresses the problem of improving the gastric retention of a swellable, controlled-release dosage form consisting essentially of a solid polymeric matrix by specifying dosage form shapes and dimensions to improve retention of the dosage form in the stomach as disclosed and claimed by the '962 Patent, and/or (ii) teaches or suggests dosage forms to one of skill in the art which consist essentially of a "solid monolithic matrix" "that swells in an unrestricted manner along both such axes" with the "shorter such axis achieving a minimum length of 1.2 cm within one hour of immersion" as recited in Claim 1 of the 962 Patent.

Validity of the '927, '989, '756, '332 and '992 Patents

5. Whether Actavis' combinations of the prior art references WO '107, WO '128, WO '812, McLean I, McLean II, Laird, Rowbotham, Magnus render obvious the asserted claims of these patents.

The evidence will show that gabapentin exhibits complex and unpredictable properties when introduced to the body that were not well-understood at the time of the inventions of the patents in suit in October 2001, and that the inventions of the patents, namely a gastric retentive dosage form with gabapentin that achieved certain therapeutic or pharmacokinetic parameters, would not have been obvious.

In fact, one of skill in the art would have been skeptical about the success of an extended-release form of gabapentin, and would have been strongly deterred from considering a gastric retained form in light of what was known at the time about gabapentin, and in light of the many uncertainties from what was not known. None of the proposed combinations of prior art would have rendered the inventions of the asserted claims obvious.

Secondary Factors

6. Whether evidence of long-felt need, skepticism, failure of others, copying and commercial success of Gralise® shows the asserted claims of these patents to be nonobvious.

The evidence will show that, despite the potential advantages of a once-daily gabapentin dosage form, there remained considerable skepticism about whether a therapeutically effective once-daily dosage form could be developed. Other well-funded pharmaceutical companies were unable to develop such a product. Some were deterred by the challenges due to the unique and unpredictable characteristics of gabapentin, and others tried and failed to develop an extended-release formulation. Depomed succeeded despite the challenges, and since its launch in October 2011, Gralise® has enjoyed commercial success. In fact, as many as six other generic companies filed ANDAs to seek to market a once-daily gabapentin product, one of which is Actavis. These secondary factors further refute Actavis' claim that Depomend's patents are invalid for obviousness.

II. BACKGROUND

This is an action for patent infringement arising under the patent laws of the United States (Title 35 of the United States Code) and arising from Defendants Actavis LLC and Actavis Elizabeth LLC (collectively, "Actavis") filing an Abbreviated New Drug Application ("ANDA") with the United States Food and Drug Administration ("FDA"), seeking approval to market a generic version of a branded Depomed product using an active ingredient known as gabapentin. The branded Depomed product, Gralise®, is a once-daily product for the management of postherpetic neuralgia (PHN) whose active ingredient is a drug called gabapentin. PHN is pain from damaged nerves that follows the healing of shingles, a painful rash caused by an infection with the herpes zoster virus. Prior to the launch of Gralise®, the only gabapentin treatments for PHN required three dosages per day.

Within just a few months after launch, Gralise® captured, and continues to capture, significant market share, confirming the strong market desire for a once-daily gabapentin product. Gralise® is covered by several U.S. patents which are listed in the Orange Book.

Defendant Actavis has sought approval from the United States Food and Drug Administration ("FDA") to sell generic gabapentin once-daily tablets. In this action Depomed asserts that Actavis infringes, and upon FDA approval and

marketing will further infringe, seven of the patents listed in the Orange Book, including: U.S. Patent Nos. 6,488,962 ("the '962 Patent"), 6,635,280 ("the '280 Patent"), 7,438,927 ("the '927 Patent"), 7,731,989 ("the '989 Patent"), 8,192,756 ("the '756 Patent"), 8,252,332 ("the '332 Patent"), and 8,333,992 ("the '992 Patent").

Actavis alleges that its ANDA and its proposed ANDA products do not infringe five of the patents (it does not contest infringement of the '332 Patent and the '992 Patent), and alleges that six of the patents are invalid as obvious. Actavis has withdrawn other alleged grounds for invalidity, although it has moved to amend its invalidity claims that the '280 Patent is indefinite.

III. JURISDICTION

The Court has subject matter jurisdiction over this action pursuant to 28 U.S.C. §§ 1331 and 1338(a). Actavis does not contest personal jurisdiction in this Action. Venue is proper in this district pursuant to 28 U.S.C. §§ 1391(b) and 1400.

IV. THE PARTIES

Plaintiff Depomed, Inc. Plaintiff Depomed, Inc. ("Depomed"), is a corporation organized under the laws of California, having its principal place of business in Newark, California. Depomed is a specialty pharmaceutical company focused on pain and other conditions and diseases of the central nervous system. Depomed's gabapentin product Gralise®, a once-daily product for the management

of postherpetic neuralgia (PHN) launched in October 2011, represents over 60% of Depomed's product sales. Depomed also developed, and receives significant licensing royalties for, its gastroretentive drug delivery technology known as Acuform®.

Defendants Actavis LLC and Actavis Elizabeth LLC. Defendant Actavis LLC is a limited liability company organized and existing under the laws of the State of Delaware, having a place of business at 60 Columbia Road, Building B, Morristown, New Jersey 07960. This entity originally was named in the complaint as "Actavis, Inc."; the entity subsequently filed a Certificate of Conversion from a Corporation to a Limited Liability Company pursuant to Section 18-214 of the Limited Liability Act with the State of Delaware, changing its name from Actavis, Inc. to Actavis LLC. *See* ECF No. 182 (Actavis' Corrected Answer to Fourth Amended Complaint). Actavis LLC was substituted as defendant in place of Actavis, Inc. on March 26, 2013. (ECF No. 162.) *Id*.

Actavis Elizabeth LLC is a wholly-owned subsidiary of Actavis LLC. Actavis Elizabeth LLC is organized and existing under the laws of the State of Delaware, having a principal place of business at 200 Elmora Avenue, Elizabeth, New Jersey 07202. Actavis Elizabeth is the named applicant on ANDA No. 203611. Actavis Elizabeth LLC's preparation and submission of ANDA No. 203611 was done collaboratively with, and for the benefit of, Actavis LLC.

V. THE RELEVANT TECHNOLOGY AND INVENTIONS

A. BACKGROUND

1. Depomed's Development of Extended Release Gabapentin

Depomed developed and markets a pharmaceutical dosage form called Gralise®, which was approved by the FDA on January 28, 2011, for treatment of post-herpetic neuralgia (PHN), or pain that may follow a herpes outbreak. The active drug in the dosage form is gabapentin, which was approved to treat epilepsy in 1993, and approved to treat PHN in 2002. Gabapentin was first approved for epilepsy in an immediate release dosage form developed by Warner-Lambert (now part of Pfizer), whose approved label required that tablets be taken three times per day. Warner-Lambert marketed the drug under the name "Neurontin." Neurontin, and subsequently approved generic formulations of gabapentin, are "immediate release" dosage forms, meaning the drug is released within minutes of ingestion.

Depomed's Gralise® is an "extended release" (sometimes called "controlled release" or "sustained release" depending upon context), gastric retained dosage form of gabapentin that is taken only once per day. A once-daily dosage regimen is preferable to multiple daily dosings because patients find once-daily doses more convenient and are less likely to forget to take a dose. In addition, a once-daily dosage may have fewer side effects and greater efficacy.

Depomed will present evidence at trial showing that the challenges of making an effective once-a-day formulation of gabapentin were daunting because

of gabapentin's unusual and uncertain properties. Depomed will provide evidence of these properties and provides a brief summary here. First, Gabapentin is absorbed primarily only in the upper gastrointestinal (GI) tract including the small intestine. Therefore, typical controlled release formulations, which release their drug throughout the entire GI tract, are not suitable.

Second, gabapentin is absorbed by a saturable mechanism, so that it saturates the "transporters" – molecules that bind to the drug and take it through the membranes of the small intestine and into the bloodstream – so that additional gabapentin cannot be absorbed. In order for gabapentin to be effective, therefore, the dosage form would need to release gabapentin not only at the correct location (the small intestine), but also at the appropriate rate in view of the saturable transporters to achieve a certain necessary rate of absorption.

Third, it was unclear whether such a formulation would be therapeutically effective. It was found, for example, that increasing the dosing frequency of gabapentin (which one normally would expect to behave similar to a controlled release formulation) resulted in unpredictable gabapentin absorption. Studies showed that gabapentin absorption improved at 4800 mg/day doses given 4 times per day, but not at 3600 mg/day given 4 times per day. These results show that one could not predict the pharmacokinetics – and thus the effectiveness – of gabapentin

from a controlled-release formulation based on the behavior of immediate release (Warner-Lambert's thrice-daily gabapentin product).

Fourth, significant inter-person variability in gabapentin absorption also cast doubt on whether an effective controlled release gabapentin formulation was possible. Variability in gabapentin absorption ranged from 5% to 74% from a 600 mg oral dose of Neurontin, suggesting that a controlled release formulation gabapentin, even if effective for some members of the population, may not be effective for many patients.

Fifth, a formulation to be taken with food appeared especially challenging. There is significant variability in gabapentin absorption depending on what type of food is present. Moreover, it was known that gabapentin can degrade to a toxic byproduct, called a lactam, and the rate of such degradation was accelerated by conditions such as with low pH (like that in the stomach), the presence of anions, the type of excipients in a dosage form, the presence of buffer, and milling of gabapentin, among others.

The challenges to making an effective sustained release gabapentin formulation is underscored by failed attempts by other companies to make such a formulation and the decision by a one prominent pharmaceutical company to develop a different drug related to gabapentin instead.

Depomed will present expert evidence by a former scientist of Warner-Lambert, the maker of Neurontin, who will testify that Warner-Lambert recognized the benefits to developing a once-daily formulation, but failed to make an effective sustained release formulation of gabapentin, despite efforts to do so. Warner-Lambert never succeeded at a controlled release gabapentin formulation, and instead pursued a formulation using "pregabalin," a gabapentin analogue, which its successor company, Pfizer, now markets as Lyrica.

[redacted].

Xenoport documented the drawbacks of gabapentin and announced that it intended to pursue a "prodrug" of gabapentin that did not have the drawbacks of gabapentin. These companies' experience and decisions further demonstrate the difficulties in making an effective controlled release dosage form.

Notwithstanding these many obstacles, and unlike the above companies, Depomed successfully demonstrated the safety and efficacy of its extended release gabapentin product for treatment of PHN through clinical trials, and the FDA

approved its product in a once-daily dosage form (in both 300mg and 600mg versions) for this indication on January 28, 2011.

On October 31, 2011, Actavis filed ANDA No. 203611 with the FDA, seeking approval to engage in the commercial manufacture, use, offer for sale, sale and/or importation of generic gabapentin once-daily tablets in 300 mg and 600 mg dosage strengths, which it represents are "bioequivalent" to Gralise®. Actavis submitted Paragraph IV Certifications to the FDA alleging that the patents identified in the Orange Book for Gralise® (including the patents in suit) are invalid, unenforceable, and/or will not be infringed by its proposed products. The FDA issued tentative approval of Actavis' ANDA, and the 30-month stay provided by the Hatch-Waxman Act expires on July 20, 2014.

B. THE PATENTS IN SUIT AND REPRESENTATIVE CLAIMS

The seven patents-in-suit can be divided into two groups: two patents that generally cover gastric retained dosage forms, and five patents that specifically cover controlled release gabapentin formulations and their methods of use. The first group of patents includes U.S. Patent Nos. 6,635,280 (the "'280 Patent") and 6,488,962 (the "'962 Patent"). The second group of patents includes U.S. Patent Nos. 7,438,927 (the "'927 Patent"), 7,731,989 (the "'989 Patent"), 8,192,756 (the "'756 Patent"), 8,252,332 (the "'332 Patent"), and 8,333,992 (the "'992 Patent").

Gastric Retention Patents ('280 and '962)

The '280 Patent, entitled "Extending the Duration of Drug Release Within the Stomach During the Fed Mode," issued to Depomed as assignee of the inventors on October 21, 2003. The patent arises from an application filed in June 1997. The '280 Patent covers oral formulations for drugs that "benefit from a prolonged time of controlled release in the stomach and upper gastrointestinal (GI) tract." Specifically, the '280 Patent is directed towards "extending the duration of drug release within the stomach during the fed mode." As explained in the patent, conventional tablets or capsules can release a highly soluble drug too quickly when they come into contact with body fluids, which results in an unwanted transient overdose followed by a period of underdosing. Also, some drugs must be absorbed higher up in the gastrointestinal tract in order to be effective. The '280 Patent addresses these and other related issues by way of gastric retained dosage forms which remain substantially intact during the period of drug release.

The patent teaches a dosage form comprising a "drug dispersed in a polymeric matrix" that "swells upon ingestion." '280 Patent, col. 5, lines 57–63. "[T]he swelling of the polymeric matrix . . . achieves two objectives – (i) the tablet swells to a size large enough to cause it to be retained in the stomach during the fed mode, and (ii) it retards the rate of diffusion of the highly soluble drug long enough

to provide multi-hour, controlled delivery of the drug into the stomach." *Id.* col. 6, lines18–24.

The '962 Patent, entitled "Tablet Shapes To Enhance Gastric Retention of Swellable Controlled-Release Oral Dosage Forms," issued to Depomed as assignee of the inventors on December 3, 2002. The application, filed in June 2000, covers an improvement over the '280 Patent by using particular shapes, sizes and swelling properties to improve gastric retention of an oral dosage form. More specifically, the '962 Patent covers "tablet shapes to enhance gastric retention of swellable controlled-release oral dosage forms." The patent teaches that dosage forms of particular shapes and sizes are both easy to swallow and resist passage through the pylorus. *See id.* col. 3, lines 22–42. "The shape that achieves this result is a non-circular, non-spherical shape which, when projected onto a planar surface, has two orthogonal axes of different lengths[.]" *Id.* col. 3, lines 27–30. An example of a shape with these characteristics is an oval. *Id.* col. 4, lines 15–16. In addition, the dosage form is of a size such that when the dosage form swells, the shorter axis of the dosage form expands to a size large enough so that it resists passage through the pylorus. *Id.* col. 4, lines 22–31.

The dosage forms covered by the '280 and '962 Patents typically include hydrophilic polymers that give the dosage form certain desired drug release characteristics. If the polymers are sufficiently hydrophilic, they will absorb

significant amounts of water when placed in an aqueous environment, such as the gastric fluid in the stomach, and thereby "swell" or increase in size.

Depomed asserts Actavis infringes Claims 1, 12, 14 and 45 of the '280 Patent under 35 U.S.C. § 271(a) and (e)(2), based on its proposed 300mg and 600mg dosage forms. Depomed asserts Actavis infringes Claims 5, 8, 10 and 13 of the '962 Patent under 35 U.S.C. § 271(a) and (e)(2), based on its proposed 600mg dosage form (Depomed does not accuse the 300mg dosage form of infringement of the '962 Patent).

Gabapentin Formulations and Methods Patents ('927, '989, '756, '332, '992)

The '927 Patent, entitled "Methods of Treatment Using a Gastric Retained Gabapentin Dosage," issued to Depomed as assignee of the inventors on October 21, 2008. The '989, '756, '332 and '992 Patents, each entitled "Gastric Retained Gabapentin Dosage Form," issued to Depomed as assignee of the inventors on June 8, 2010, June 5, 2012, August 28, 2012, and December 18, 2012, respectively. All five patents arise from a common Provisional Application No. 60/335,248, filed on October 25, 2001, and the applications that resulted in these five patents are continuations of each other. Accordingly, all five patents share the same specification.

The '927, '989, '756, '332 and '992 Patents generally cover gastric retained gabapentin dosage forms and methods of using the same. As a gastric retained

dosage form, the gabapentin dosage form resides longer in the stomach and thereby ensures that gabapentin is released primarily in the stomach and the upper gastrointestinal tract, and not in the colon. This is critical as gabapentin is primarily absorbed in the ***upper*** gastrointestinal tract of a patient and not in the lower gastrointestinal tract, such as the colon. (*See, e.g.*, '927 Patent, Col. 1, ll. 43-50.) The gastric retained gabapentin dosage form covered by the patents-in-suit is thus superior to extended release formulations, which would otherwise release gabapentin throughout the gastrointestinal tract and would therefore not be effective. *See, e.g.*, '927 Patent, col. 1, lines 25-36, col 2, lines 14-25.

As a controlled/sustained release formulation, the dosage form taught in the patents overcomes the drawbacks of immediate-release dosage forms of gabapentin, such as Neurontin®, which have a comparatively higher incidence of side effects. The patents also are directed to methods of treating conditions specifically responsive to gabapentin – epilepsy and neuropathic pain – using the gastric retained dosage forms. *Id.* at col 1, lines 54-64.

Based on Actavis' proposed 300 mg and 600mg dosage forms, Depomed asserts Actavis infringes Claims 18, 25, 26, 34, 61 and 62 of the '927 Patent under 35 U.S.C. § 271(b) & (c) and (e)(2); Claim 10 of the '989 Patent under 35 U.S.C. § 271(a) and (e)(2); Claims 1, 2, 5, 6, 7 and 11 of the '756 Patent under 35 U.S.C. § 271(a) and (e)(2) and additionally Claims 6, 7 and 11, under § 271(b) & (c);

Claims 1, 6, 17, 22 and 24 of the '332 Patent under 35 U.S.C. § 271(a), (b), (c), and (e)(2) (not contested); and Claims 1, 5 and 22 of the '992 Patent under 35 U.S.C. § 271(a), (b), (c), and (e)(2) (not contested).

C. CLAIM CONSTRUCTION

The Court issued its claim construction order on January 28, 2014, construing disputed claim terms. ECF No. 251. A summary of the constructions in that order, as well as stipulated constructions, is attached hereto as Exhibit A.

VI. LEGAL ISSUES TO BE DECIDED

Actavis has stipulated that its 300mg and 600mg dosage forms, when used according to their indicated use, meet all elements of the asserted claims of the '332 and '992 Patents. Thus, infringement of these patents is not disputed. Depomed refers the Court to the statement of legal issues in the pretrial order.

VII. KEY FACTS TO BE DETERMINED

A. INFRINGEMENT

The parties have significantly narrowed the infringement issues by stipulation. *See* Supplemental Stipulated Facts and Issues filed April 30, 2014, as a Supplement to Exhibit 1 to Joint Proposed Pretrial Order. For two of the patents ('332 and '992), Actavis stipulates that its 300mg and 600mg dosage forms, when used according to their indicated use, meet all elements of the asserted claims. Thus, Actavis does not contest infringement of these two patents.

For each of the five other patents, Actavis disputes only one claim element, as set forth below:

1. ***'280 Patent***. The sole infringement issue for this patent is whether Actavis' 300mg and 600mg dosage forms include this claim element: "said dosage form being one that when swollen . . . is of a size exceeding the pyloric diameter in the fed mode to promote retention in the stomach during said fed mode." The Court has construed this element to mean the dosage form is swollen "such that when the dosage form is introduced into the stomach in the fed mode, the dosage form remains in the stomach for several hours." *See* Exhibit A (Claim Construction Summary).

2. ***'962 Patent***. The sole infringement issue for this patent is whether Actavis' 600mg dosage form includes this claim element: "wherein said matrix has a shape which when projected onto a plane, is either an oval or a parallelogram." The parties have agreed this claim element means "any curve that is closed and concave towards the center wherein the geometric form bounded by the closed curve has a first and second orthogonal axes of unequal length." *See* Exhibit A. (Depomed does not assert that Actavis' 300mg dosage form infringes this patent).

3. ***'927 Patent***. The sole infringement issue for this patent is whether Actavis' 300mg and 600mg dosage forms include this claim element: "swells . . . to increase its size to promote gastric retention of the dosage form in the stomach of the mammal." The Court has construed this element to mean the dosage form swells "such that when the dosage form is introduced into the stomach, the dosage form remains in the stomach for several hours." *See* Exhibit A.

4. ***'989 Patent***. The sole infringement issue for this patent is whether Actavis' 300mg and 600mg dosage forms include this claim element: "swells . . . to increase its size to promote gastric retention of the dosage form in a stomach in a fed mode." The Court has construed this element to mean that the dosage form swells "such that when the dosage form is introduced into the stomach in the fed mode, the dosage form remains in the stomach for several hours." *See* Exhibit A.

5. ***'756 Patent***. The sole infringement issue for this patent is whether Actavis' 300mg and 600mg dosage forms include this claim element: "swells . . . to increase its size to promote gastric retention of the dosage form in the stomach in a fed mode." The Court has construed this element to mean that the dosage form swells "such that when the dosage form is introduced into the stomach in the fed mode, the dosage form remains in the stomach for several hours." *See* Exhibit A.

Except for the '332 and '992 Patents (the infringement of which Actavis does not contest) and the '962 Patent (which involves the shape of the tablets), Actavis' defense to the asserted patent claims is based solely on its dispute whether its products "remain in the stomach for several hours" – that is, whether its products are gastrically retained.

Depomed asserts that Actavis contributorily infringes, or will contributorily infringe, the '927 Patent and the '756 Patent. Facts to be determined relevant to this issue include whether there is, or will be, a direct infringement by physicians or others using Actavis' proposed dosage forms, and whether Actavis' proposed dosage forms have a substantial noninfringing use.

Depomed asserts that Actavis also induces infringement, or will induce infringement, of the '927 Patent and the '756 Patent. Facts to be determined relevant to this issue include whether Actavis knowingly induces, or will knowingly induce, infringement by others and whether Actavis has the intent to encourage infringement by others.

B. VALIDITY

Actavis has withdrawn assertions that the '280 Patent is invalid due to obviousness, and presently has no claims that the '280 Patent is invalid. However, as noted above, Actavis recently filed a Motion to Amend Invalidity Contentions to add an assertion that the '280 Patent is indefinite, which is a question of law. If Actavis' motion to amend is denied, Actavis has no claim of invalidity as to the '280 Patent.

The only ground on which Actavis alleges the other six patents in suit are invalid is obviousness under 35 U.S.C. § 103, *supra*. For the gabapentin patents below, Depomed summarizes the three prior art references upon which Actavis primarily relies and the key facts relevant to Actavis' obviousness defense. Actavis' primary assertion is that references teaching drug formulations using gastric retention combined with references allegedly teaching immediate release gabapentin render the patents obvious.

WO 98/55107 ("WO '107"). WO '107, entitled "Gastric-retentive oral drug dosage forms for controlled release or highly soluble drugs," was published on December 10, 1998. The listed inventors are John W. Shell and Jenny Louie-Helm and is based on work at Depomed. WO '107 teaches gastric retained dosage forms for highly water soluble drugs. There are over 200 highly water soluble drugs listed in the pharmacopeia. *WO '107 does not teach gabapentin, any*

pharmacokinetic parameters or a method of treating any condition with gabapentin.

Because WO '107 makes no mention of gabapentin, Actavis relies on combinations with prior art references that disclose the therapeutic effects of immediate release gabapentin based on articles published in the 1990s by M. Rowbotham, McLean I, McLean II, Laird and Magnus.

The evidence will show that gabapentin's properties rendered unpredictable the pharmacokinetics, and the therapeutic efficacy to expect from a controlled release, gastrically retained, oral gabapentin dosage form as set forth in the claimed inventions. The properties that contributed to the unpredictability included: (a) unpredictable gabapentin dose-absorption kinetics; (b) potential degradation of gabapentin in the acidic stomach environment; (c) the need for appropriate rate of release of gabapentin at the appropriate site from the dosage form to ensure optimal absorption; (d) unpredictable effect of food on gabapentin absorption; and (e) inter-person variability. Thus, depending on the type of dosage form, gabapentin release from the dosage form and its absorption and concomitantly the pharmacokinetics could be entirely different. The unpredictability in pharmacokinetics also rendered unpredictable the therapeutic efficacy of the controlled release, gastrically retained oral dosage form of the inventions claimed.

WO 99/47128 ("WO '128"). WO '128 teaches a gastric retained dosage form, and specifically discloses metformin as an example drug. Like WO '107, WO '128 does not disclose pharmacokinetic values of gabapentin from any dosage form, let alone from a gastrically retained controlled release dosage form with gabapentin. WO '128 also fails to disclose that gabapentin released from a gastrically retained, controlled release dosage form must have a lower C_{max}, higher T_{max} and at least 80% bioavailability as that from an immediate release dosage form of gabapentin. WO '128 does disclose a single example of pharmacokinetic parameters for metformin.

Actavis relies on WO '128 in combination with the gabapentin references discussed above, to allege that the asserted claims of the '756 Patent, the '332 Patent and the '992 Patent (directed to dosage forms of gabapentin in a polymer matrix) are obvious. Actavis claims that one of skill in the art would have been motivated to make a controlled release formulation of gabapentin using the dosage form disclosed in WO '128, even though that reference does not mention gabapentin.

As discussed above, however, the evidence will show that the unique characteristics of gabapentin would have discouraged one of skill from trying to make a gastrically retained formulation with gabapentin. Moreover, metformin and gabapentin are different chemicals with very different properties.

WO 01/37812. WO '812 teaches a drug delivery system that is "a combination system, comprising at least two components, namely the matrix and the membrane affixed or attached thereto. Taken separately, neither the matrix nor the membrane would retain in the stomach more than a conventional dosage form." Thus, the matrix disclosed in WO '812 is not gastrically retained when it is without the membrane. "However, when the membrane is affixed or attached to the matrix, it prevents evacuation of the matrix for the desired period of time. At the same time, the matrix, when the membrane is affixed or attached thereto, prevents, for the desired period of time, the so termed 'collapse' of the membrane, which would have led to its rapid evacuation from the stomach." WO '812 discloses gastroretentive dosage form (GRDF) containing riboflavin and includes gabapentin in its laundry list of potential drugs that "may" be suitable for use in the dosage form. This piece of prior art is asserted against the '992 and '332 Patents.

In addition, the evidence will show numerous secondary factors that show the asserted claims are not obvious. Depomed will present expert testimony showing the skepticism in the industry regarding a successful extended release formulation of gabapentin, the failure of others to develop such a dosage form, and the commercial success of Depomed's Gralise® product in its first two years on the market.

VIII. RELEVANT AUTHORITY AND ARGUMENT

A. OBVIOUSNESS

Defendants claim that each of the asserted claims are invalid due to obviousness under 35 U.S.C. §103. Because every claim of an issued patent is independently presumed valid, the burden of proving invalidity by clear and convincing evidence falls to the party challenging the validity of the patent. *Microsoft Corp. v. i4i Ltd. Partnership,* 131 S.Ct. 2238, 2243 (2011); *See* 35 U.S.C. § 282. Clear and convincing evidence should "instantly tilt[ ] the evidentiary scales" in favor of its proponent when weighed against the opposing evidence. *Colorado v. New Mexico*, 467 U.S. 310, 316 (1984).

Prior art analyzed for the invalidity challenge must be viewed from the perspective of a hypothetical person of ordinary skill in the art ("POSA") at the time the invention was made and must consider aspects of the prior art that might lead away from the claimed invention. *See* 35 U.S.C. § 103(a); *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406, (2007); *In re Dow Chem. Co.*, 837 F.2d 469, 473 (Fed.Cir.1988).

The Federal Circuit has warned that hindsight must be avoided in the obviousness analysis. This is avoided by requiring the challenging party to explain "how or why the references would be combined to produce the claimed invention." *Innogenetics, N.V. v. Abbott Laboratories,* 512 F.3d 1363, 1374 n. 3

(Fed.Cir.2008). A patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *KSR*, 550 U.S. at 418. The prior art provided by the Defendants fails to teach crucial elements found in the asserted claims of the asserted patent and would not motivate a person of ordinary skill in the art to combine the references with any expectation of success. The Defendants fail to show by clear and convincing evidence that the asserted claims are obvious.

B. INDEFINITENESS

Defendants have filed a motion *in limine* to add the recent claim of indefiniteness as to the term "is of a size exceeding the pyloric diameter in the fed mode to promote retention in the stomach during said fed mode" from the '280 Patent. This legal issue need only be decided if the Court grants this motion.

The amount of claim detail necessary is to satisfy the definiteness requirement of 35 U.S.C. § 112 is dependent upon the scope of the claims, the complexity of the subject matter, and the understanding of the person of ordinary skill in the art. *Miles Labs., Inc, v. Shandon Inc.*, 997 F.2d 870, 875 (Fed. Cir. 1983). Courts examine and review the scope of the claims as a matter of law, but review the other two definiteness variables as questions of fact. *BJ Servs. Co. v. Halliburton Energy Servs. Inc.*, 338 F.3d 1368, 1372 (Fed. Cir. 2003). A court looks to the disclosure of the patent, and the intrinsic evidence, to decide

indefiniteness. *ePlus, Inc. v. Lawson Software, Inc.*, 700 F.3d 509,519 (Fed. Cir. 2012).

A decision on whether a claim is invalid under § 112, ¶2, requires a determination of whether those skilled in the art would understand what is claimed when the claim is read in light of the specification. *Orthokinetics, Inc. v. Safety Travel Chairs, Inc*., 806 F.2d 1565, 1576 (Fed. Cir. 1986) (finding that the claims were not indefinite because a person of ordinary skill in the art would be able to determine the appropriate dimensions based on the specification and that the claim phrase was as accurate as the subject matter permitted) *citing Seattle Box Co. v. Industrial Crating & Packing Inc.*, 731 F.2d 818, 826 (Fed. Cir. 1984). A patent is indefinite only if it is "not amenable to construction" or "insolubly ambiguous." *Exxon Research & Eng'g Co. v. United States*, 265 F.3d 1371, 1375 (Fed. Cir. 2001).

This phrase is not only amenable to construction, but has been construed by this Court, Judge Hamilton, Judge Breyer, and by the Defendants in their claim construction brief in this case. The Courts that have reviewed this language have construed it to mean "such that when the dosage form is introduced into the stomach in the fed mode, the dosage form remains in the stomach for several hours." As such, there is no reason to now decide that this phrase is indefinite.

Notably, Judge Breyer of the Northern District of California explained that a special meaning need not be ascribed to this claim term, which is found in the '280 Patent claims, but not in the now unasserted '475 Patent claims:

> Court is unpersuaded that the specific language in the '280 patent regarding the expansion of the dosage form to a 'size exceeding the pyloric diameter' should render the meaning of that term different in substance from the term in 475 patent, which refers only more generally to a 'size large enough to promote retention in the stomach.' Indeed, the equivalence of these two phrases is evident from the plain language of the '280 patent itself, which suggests that a swollen dosage form must achieve a size exceeding the pyloric diameter precisely in order to promote its retention in the stomach.

ECF No. 138-2, Ex. 10 (Judge Breyer's Construction) at 16.

C. CONTRIBUTORY INFRINGEMENT

If Actavis' ANDA product is marketed, Actavis will contribute to the infringement of the method claims found in claims 17 and 33 of the '927 Patent, claim 6 of the '756 Patent, claim 12 and 24 of the '332 Patent, and claims 22 of the '992 Patent, as well as the claims dependent upon these claims, under 35 U.S.C. § 271(b). These method claim and their dependent claims cover the use of the described dosage form in "neuropathic pain" (claim 17 of the '927 Patent, claim 11 of the '756 Patent, and 17 of the '332 Patent), a "condition responsive to a therapeutic dose of gabapentin" (claim 6 of the '756 Patent, claim 24 of the '332 Patent, and claim 22 of the '992 Patent) and "administering a therapeutically effective amount of . . . gabapentin" (claim 33 of the '927 Patent).

A party is liable for contributory infringement if: (1) there is direct infringement; (2) the accused infringer had knowledge of the patent at issue; (3) the component has no substantial noninfringing uses; and (4) the component is a material part of the invention. *Bone Care v. Roxane* citing *Fujitsu Ltd. v. Netgear Inc.*, 620 F.3d 1321, 1326 (Fed. Cir. 2010); *Lucent Techs. Inc. v. Gateway, Inc.*, 580 F.3d 1301, 1320 (Fed. Cir. 2009); 35 U.S.C. § 271(c). A product is a material component of a composition when it is the sole physical object necessary to practice the method claim. *Braintree Labs, Inc. v. Novel Labs, Inc.*, 2013 WL 211252 at *13 (Jan. 18, 2013 D.N.J.). The defendant bears the burden of proving substantial non-infringing uses. *University of California v. Hansen*, 54 U.S.P.Q.2d 1473, 1480 (E.D.Cal.1999)

Actavis' filing of its ANDA 203611 demonstrates that it was aware of the patents and will be aware of the patents when and if it markets its Acatavis ANDA product. Actavis has stipulated to infringement of at least the '332 and '992 Patents and that its dosage forms meet all but one of the claim elements of the remaining patents. The sole physical object necessary to practice the method claims of the asserted patents is the Gralise® dosage form which the Actavis ANDA product mimics in design, function and through its label providing instructions for use. The only use described in the proposed labeling for the Actavis ANDA product is one matching the method patents and, in any event, the

claims cover all therapeutic uses. Therefore, the Actavis will contribute to infringement if it markets its Actavis ANDA product.

D. INDUCED INFRINGEMENT

If Actavis' ANDA product is marketed, Actavis will induce the infringement of the method claims found in claims 17 and 33 of the '927 Patent, claim 6 of the '756 Patent, claim 12 and 24 of the '332 Patent, and claims 22 of the '992 Patent, as well as the claims dependent upon these claims, under 35 U.S.C. § 271(b). These method claim and their dependent claims cover the use of the described dosage form in "neuropathic pain" (claim 17 of the '927 Patent, claim 11 of the '756 Patent, and 17 of the '332 Patent), a "condition responsive to a therapeutic dose of gabapentin" (claim 6 of the '756 Patent, claim 24 of the '332 Patent, and claim 22 of the '992 Patent) and "administering a therapeutically effective amount of . . . gabapentin" (claim 33 of the '927 Patent).

A party is liable for inducement of infringement under 35 U.S.C. § 271(b) if it is shown that: (1) the alleged infringer was aware of the patent (2) it knowingly induced infringement and (3) it possessed specific intent to encourage another's infringement." *Symantec Corp. v. Computer Assocs. Int'l, Inc.*, 522 F.3d 1279, 1292 (Fed. Cir. 2008) (quoting *MEMC Elec. Materials, Inc. v. Mitsubishi Materials Silicon Corp.*, 420 F.3d 1369, 1378 (Fed. Cir. 2005)). *See also DSU Med. Corp. v. JMS Co., Ltd.*, 471 F.3d 1293, 1305–06 (Fed.Cir.2006) (*en banc*)

(finding that inducement requires another party directly infringes the claim; the party intentionally encourages the acts that constitute direct infringement; and the party knows or should know that its actions will cause direct infringement). A defendant who is aware of a patent and supplies a product to a customer with instructions on how to use the product, which instructions when followed lead to infringement, encourages acts which constitute direct infringement. *Minn. Mining and Mfg. Co. v. Chemque, Inc.,* 303 F.3d 1294, 1305 (Fed.Cir.2002). *See also Biotec Biologische Naturverpackungen GmbH & Co. v. Biocorp, Inc.,* 249 F.3d 1341, 1351 (Fed.Cir.2001) (defendant induced infringement by providing instructions to customers on how to use a product in a manner that constituted direct infringement). Circumstantial evidence, such as including instructions in a "proposed label that will cause at least some users to infringe the asserted method claims can prove specific intent to cause direct infringement." *Allergan v. Apotex* citing *AstraZeneca LP v. Apotex, Inc.,* 633 F.3d 1042, 1060 (Fed. Cir. 2010); *see* 35 U.S.C. § 271(b).

A comparison between an accused product and a commercial embodiment of a patented product can be used to establish infringement where the commercial product demonstrates the presence of the relevant claim limitations. *Glaxo Group, Ltd. v. TorPharm, Inc.,* 153 F.3d 1366, 1374 (Fed.Cir.1998). Actavis has stipulated that the Gralise® Tablets are embodiments of the asserted claims of the

'927, 989, '756, '332, 'and '992 Patents, which include the asserted method patents. Actavis has copied the label for the use of Gralise® with only minor modifications that do not change the instructions for the use of the tablets. Actavis' copying of a dosage form whose composition and use admittedly fall within the parameters of the asserted claims proves that Actavis is liable for induced infringement under 35 U.S.C. § 271(b).

E. ACTAVIS'S EXPECTED ATTEMPT TO PROFFER WHOLLY NEW EXPERT TESTIMONY ON INFRINGEMENT OF THE '962 PATENT THAT IT FAILED TO DISCLOSE WAS A DISPUTED ELEMENT IN ITS LOCAL PATENT RULE DISCLOSURES

Depomed anticipates that Actavis's shifting non-infringement position with regard to the "oval or parallelogram" element of Claim 1 of the '962 Patent[1] will require the Court to rule on the admissibility of expert testimony offered for the first time at trial. Actavis foreshadowed as much by including previously undisclosed facts in its opposition to Depomed's Motion *in Limine* No. 3 that assertedly demonstrate why the 600 mg Actavis Tablet falls outside of the stipulated construction of "an oval." (*See* ECF No. 308 at 4, second paragraph and fn. 4; at 5, first paragraph; and at 6, first paragraph.) Actavis suggests that it will adhere to the stipulated construction. (*Id.* at 2.)

[1] The parties stipulated one year ago to a construction of the claim term "an oval" first issued by Judge Hamilton in *Lupin* and then confirmed by this Court in *Sun*. ECF No. 188-1 at A-3 (Exhibit A to Revised Joint Claim Construction and Prehearing Statement).

At the outset, Actavis never stated in its Non-Infringement Contentions that it would affirmatively dispute that its ANDA products infringe this element. ECF No. 278-1(Actavis Non-Infringement Contentions served Aug. 24, 2012) at 10. As such, any evidence should be precluded as a violation of the local patent rules. *See, e.g.*, *Sanofi-Aventis v. Barr Labs., Inc.*, 598 F.Supp.2d 632, 637 (D.N.J. 2009) ("Local Patent Rule 3.6 requires ***ultra*** early disclosure of infringement and invalidity contentions for patent cases arising under the Hatch-Waxman Act.") (emphasis in original); *Janssen Prods., L.P. v. Lupin Ltd.*, Case No. 10-5954, 2013 WL 3086378, at * 2 (D.N.J. June 18, 2013) ("Because this action arises under the Hatch-Waxman Act, it is even more imperative that the parties establish their contentions early" so that the parties and their experts can "fully explore[] and scrutinize[]" those contentions).

Further, it would be improper for Actavis to attempt to present this evidence for the first time at trial because such scientific or technical knowledge should have been disclosed to Depomed during expert discovery. *Dunkin' Donuts, Inc., v. Patel*, 174 F. Supp. 2d 202, 211 (D.N.J. 2001); *see* Fed. R. Civ. P. 26(a)(2)(B). In evaluating whether a non-disclosure warrants exclusion, the Third Circuit has identified four factors to consider: "(1) the prejudice or surprise of the party against whom the excluded evidence would have been admitted; (2) the ability of the party to cure the prejudice; (3) the extent to which allowing the evidence would

disrupt the orderly and efficient trial of the case or other cases in the court; and (4) bad faith or willfulness in failing to comply with a court order or discovery obligation." *Nicholas v. Pa. State Univ.*, 227 F.3d 133, 148 (3d Cir. 2000). The party who fails to disclose information bears the burden of showing that the nondisclosure was substantially justified or is harmless. *See D & D Assoc.*, 2006 WL 1644742, at *4. (June 8, 2006 D.N.J). Exclusion of the expert's opinion from trial is appropriate where the expert's opinion is incomplete, changes, or is late. *Waddington North American, Inc. v. Sabert Corp.*, 2011 WL 1098997 at *7 (March 22, 2011 D.N.J.) (finding that the expert's late declaration would be excluded because it was prejudicial and could not be otherwise cured a week before trial).

In any event, such evidence does not alter the fact that the 600 mg Actavis Tablet is indeed "an oval," *i.e.*, "any curve that is closed and concave towards the center wherein the geometric form bounded by the closed curve has a first and second orthogonal axes of unequal length." *First*, the evidence will show that the matrix projected by the ANDA product (as the element requires) does indeed fall within the stipulated construction. *Second*, the evidence will also show that Depomed did not disclaim tablet shapes that meet this construction during prosecution, as Actavis asserts, because the amendment including the "oval" limitation was made without elaboration. *Third*, the evidence will show that

Depomed referenced tablet literature from Elizabeth Carbide during the *Lupin* claim construction proceedings in order to distinguish ovals from capsules with ***straight*** edges. The projection of the 600 mg Actavis Tablet is rounded at all points. *Fourth*, additional tablet shapes introduced for the first time in Actavis's *in limine* opposition can be squared with the stipulated construction, as Depomed will establish if necessary. For at least these reasons, Actavis's belated attempt to buttress its noninfringement position as to "an oval" is untenable.

IX. CONCLUSION

For all these reasons and the evidence to be adduced at trial, Depomed requests that judgment be granted in its favor.

Dated: May 2, 2014

Respectfully submitted,

By: /s/ *Leda Dunn Wettre*

Leda Dunn Wettre
ROBINSON, WETTRE & MILLER LLC
One Newark Center, 19th Floor
Newark, New Jersey 07102
Telephone: (973) 690-5400
Facsimile: (973) 466-2760
Email: lwettre@rwmlegal.com

Attorneys for Plaintiff Depomed, Inc.

CERTIFICATE OF SERVICE

I hereby certify under penalty of perjury that a true copy of the attached was filed with the Court and served upon all counsel of record via CM/ECF.

Dated: May 2, 2014

Leda Dunn Wettre
Leda Dunn Wettre